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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2003

Effective 01/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small status. See 37 CFR 1.27

Total Amount of Payment ($)320.00

Complete if Known	
Application Number	09/872,731
Filing Date	June 1, 2001
First Named Inventor	Matthew Merrill Hayward, et al.
Examiner Name	Liu, Hong
Art Unit	1624
Attorney Docket No.	PC11032A

METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit Card ☐ Money Order ☐ Other ☐ None

☒ Deposit Account:

Deposit Account Number: 16-1445

Deposit Account Name: Pfizer Inc.

The Commissioner is authorized to: (check all that apply)

☒ Charge fee(s) indicated below ☒ Credit any overpayments

☐ Charge any additional fee(s) during the pendency of this application

☐ Charge fee(s) indicated below, **except for the filing fee** to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	750	2001	375	Utility filing fee	
1002	330	2002	165	Design filing fee	
1003	520	2003	260	Plant filing fee	
1004	750	2004	375	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($)

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

			Extra Claims		Fee from below		Fee Paid
Total Claims		-20**=		X		=	
Independent Claims		- 3**=		X		=	
Multiple Dependent						=	

*** or number previously paid, if greater; For Reissues, see below*

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	84	2201	42	Independent claims in excess of 3
1203	280	2203	140	Multiple dependent claim, if not paid
1204	84	2204	42	**Reissue independent claims over original patent
1205	18	2205	9	**Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($)

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge – late fee or oath	
1052	50	2052	25	Surcharge–late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	410	2252	205	Extension for reply within second month	
1253	930	2253	465	Extension for reply within third month	
1254	1,450	2254	725	Extension for reply within fourth month	
1255	1,970	2255	985	Extension for reply within fifth month	
1401	320	2401	160	Notice of Appeal	
1402	320	2402	160	Filing a brief in support of an appeal	320.00
1403	280	2403	140	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,300	2453	650	Petition to revive - unintentional	
1501	1,300	2501	650	Utility issue fee (or reissue)	
1502	470	2502	235	Design issue fee	
1503	630	2503	315	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17 (q)	
1801	750	2801	375	Request for Continued Examination (RCE)	
1806	180	1806	180	Submission of Information Disclosure Statement	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	750	2809	375	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	750	2810	375	For each additional invention to be examined (37 CFR 1.129(b))	
				Other Fee (specify)	

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 320.00

SUBMITTED BY				Complete (if Applicable)	
Name (Printed/Type)	Scott Alexander McNeil			Reg. Number	37,185
Signature	Scott Alexander McNeil	Date	16 June 2003	Telephone	(860)686-1848

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#12

Patent
Application
Docket No.
PC11032A

I hereby certify that this correspondence is being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Hon. Commissioner for Patents, Washington, D.C. 20231 on this 16th day of June, 2003.

By Kelly A. Smith
(Signature of person mailing)
Kelly A. Smith
(Typed or printed name of person)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:
Mathew Merrill Hayward *et al.*

Serial No.: 09/872,731
Filed: June 1, 2001

Group Art Unit: 1624

Examiner: LIU, HONG

For: HYGROMYCIN A DERIVATIVES

BRIEF ON APPEAL

Commissioner for Patents
Washington, DC 20231

Dear Sir:

By Notice of Appeal, filed April 11, 2003, Appellants have appealed the Final Rejection, dated February 12, 2003, of Claims 1-8. Appellants submit this Brief, in triplicate, to support the Notice of Appeal.

Payment authorization, for filing this Brief On Appeal, is provided by the concurrently filed Transmittal Letter.

I. Real Party in Interest

The present application, listing the inventors Mathew Merrill Hayward, Michael S. Visser, Robert G. Linde II and Takushi Kaneko, is owned in its entirety by Pfizer Inc.

II. Related Appeals and Interferences

There are no other appeals or interferences, known to Appellants or Appellants' Attorney, relating to the present application, which will directly affect, be directly affected by, or have a bearing on the Board's decision on the pending appeal.

III. Status of Claims

Claims 1-8 are currently pending in the present application. Claims 1-8, which are attached as Appendix A, are final rejected under 35 USC 112, first paragraph. Claims 1-8 also stand final rejected under 35 USC 103.

IV. Status of Amendments

No amendments have been filed in the present application subsequent to the final rejection.

V. Summary of the Invention

The present invention, as claimed in independent Claim 1, is directed to compounds, which are derivatives of hygromycin A, or a pharmaceutically acceptable prodrug, salt or solvate thereof.

The invention of Claim 7 is directed to a pharmaceutical composition comprising a compound of Claim 1 and a pharmaceutically acceptable carrier.

The invention of Claim 8 is directed to a method of treating a bacterial infection, a protozoal infection or a disorder related to a bacterial infection or protozoal

infection comprising administering a therapeutically effective amount of a compound of Claim 1.

VI. Issues

A. Whether Claims 1-8 are properly rejected under 35 USC 112, first paragraph.

B. Whether Claims 1-8 are obvious, under, 35 USC 103(a), over U.S. Patent No. 6,245,745.

VII. Grouping of Claims

Claims 1-8 are one group. It is respectfully requested that the Board select Claim 1 to decide the appeal as to the grounds of the rejection of Claims 1-8.

VIII. Argument

A. A Rejection, Under 35 USC 112, First Paragraph, for not Enabling One Skilled in the Art to Determine How the Prodrug is Converted to the Active Drug In Vivo, Is Not Proper

Claims 1-8 are rejected under 35 USC 112, first paragraph. The Examiner stated, in first making this rejection, that the scope of "prodrug" is not adequately enabled because guidance was not provided as to how the compounds are made more active *in vivo*. In the final rejection, the Examiner more specifically stated that the term "prodrug", as defined in Appellants' application is broad and that the Appellants' application does not enable one skilled in the art to determine how the prodrug is converted to active compounds, by what mechanisms and at what site the prodrug will be activated and what *in vivo* enzymes are more likely involved in cleaving the protected group.

Contrary to the Examiner's statement, the term "prodrug" is suitably enabled in the present application. It is well known in the art that typical prodrugs of compounds having free amino, amido, hydroxy or carboxylic groups of the compound, will readily form said compound *in vivo*. Thus, to enable the invention of Claims 1-8, Applicants are not required to provide guidance on the mechanism or the site in the body that the prodrug is converted *in vivo* to form the active compound.

Thus, pending Claims 1-8 are improperly rejected as being non-enabling.

B. An Obviousness Rejection, Under 35 USC 103(a), Is Not Proper Where There Is Common Ownership at the Time of Invention (35 USC 103(c)).

Claims 1-8 are rejected under 35 USC 103(a) as being unpatentable over US Patent No. 6,245,745. The Examiner stated that once a patent is published, the patent can be used as prior art of the filing date of the patent. This would appear to be a 102(e)/103 rejection.

The Examiner also stated that the present application and US 6,245,745 have different inventive entities.

Contrary to the Examiner's statement, US 6,245,745 is not valid prior art for the claims in the present patent application in that US 6,245,745 does not constitute valid prior art under 35 U.S.C. Sections 102(e).

35 USC 103(c) states:

> "Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this

section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person."

At the time the Appellants' invention, which is recited in the present application USSN 09/872,731, was made, US 6,245,745 was owned by Pfizer Inc.

Further, at the time the Appellants' invention, recited in USSN 09/872,731, was made, said invention was subject to an obligation of assignment to Pfizer Inc. At the time of invention, Mathew Merrill Hayward, Michael S. Visser, Robert G. Linde II and Takushi Kaneko were Pfizer employees with a contractual duty to assign to Pfizer Inc. inventions made in the employ of Pfizer Inc.

Thus, pending Claims 1-8 are improperly rejected as being obvious under 35 USC 102(e)/103 in view of US 6,245,745.

IX. Conclusion

In view of the above information, present Claims 1-8 are not properly rejected under 35 USC 112, first paragraph, or under 35 USC 103(a). Therefore, it is respectfully requested that the rejection of Claims 1-8 be withdrawn and that Claims 1-8 be allowed.

Date: 16 June 2003

Respectfully submitted,

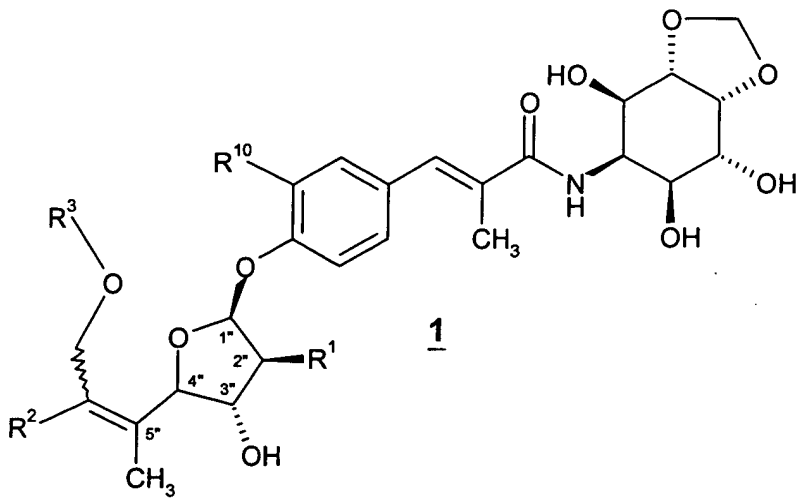
Scott Alexander McNeil

Scott Alexander McNeil
Attorney for Appellants
Reg. No. 37,185

APPENDIX A

Claims Under Appeal

1. A compound of the formula



1

or a pharmaceutically acceptable prodrug, salt or solvate thereof wherein:

each R^1 and R^{10} is independently H or OH;

R^2 is H or C_1-C_6 alkyl wherein the foregoing R^2 alkyl group is optionally substituted by 1 or 2 R^4 groups;

each R^3 is independently selected from C_6-C_{10} aryl or 5 to 10 membered heteroaromatic, and the heteroaromatic and aryl moieties of the foregoing R^3 groups are substituted by a $-CHR^9NR^{11}R^{12}$ group and optionally substituted by 1 to 4 R^4 groups;

each R^4 is independently selected from, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, halo, cyano, nitro, trifluoromethyl, difluoromethyl, trifluoromethoxy, azido, hydroxy, C_1-C_6 alkoxy, $-C(O)R^5$, $-C(O)OR^5$, $-NR^6C(O)OR^8$, $-OC(O)R^5$, $-NR^6SO_2R^8$, $-SO_2NR^5R^6$, $-NR^6C(O)R^5$, $-C(O)NR^5R^6$, $-NR^5R^6$, $-S(O)_j(CR^6R^7)_m(C_6$-C_{10} aryl), $-S(O)_j(C_1$-C_6 alkyl), $-(CR^6R^7)_m(C_6$-C_{10} aryl), $-O(CR^6R^7)_m(C_6$-C_{10} aryl), $-NR^6(CR^6R^7)_m(C_6$-C_{10} aryl), $-(CR^6R^7)_m$(4 to 10 membered heterocyclic), $-C(O)(CR^6R^7)_m(C_6$-C_{10} aryl), and $-C(O)(CR^6R^7)_m$(4 to 10 membered heterocyclic), wherein m is an integer from 0 to 4; j is an integer from 0 to 2, and said alkyl, alkenyl, alkynyl, aryl and heterocyclic moieties of the foregoing R^4 groups are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, $-NR^6SO_2R^8$, $-SO_2NR^5R^6$, $-C(O)R^5$, $-C(O)OR^5$, $-OC(O)R^5$, $-NR^6C(O)OR^8$, $-NR^6C(O)R^5$, $-C(O)NR^5R^6$, $-NR^5R^6$, $-OR^5$, C_1-C_{10} alkyl, $-(CR^6R^7)_m(C_6$-C_{10} aryl), and $-(CR^6R^7)_m$(4 to 10 membered heterocyclic), wherein m is an integer from 0 to 4;

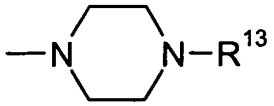
each R^5, R^9, R^{11}, R^{12}, R^{13} and R^{14} is independently selected from H, C_1-C_{10} alkyl, $-(CR^6R^7)_m(C_6$-C_{10} aryl), $-(CR^6R^7)_m(C_3$-C_{10} cycloalkyl), indanyl and $-(CR^6R^7)_m$(4 to 10 membered heterocyclic), wherein m is an integer from 0 to 4, and the foregoing R^5 , R^{11}, R^9 and R^{12}

substituents, except H, are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, benzyl, trifluoromethyl, trifluoromethoxy, azido, $-CH_2(C_2-C_6$ alkenyl), $-C(O)R^6$, $-C(O)OR^6$, $-OC(O)R^6$, $-NR^6C(O)R^7$, $-C(O)NR^6R^7$, $-NR^6R^7$, hydroxy, C_1-C_6 alkyl, and C_1-C_6 alkoxy;

or R^{11} and R^{12} can be taken together to form a 4 to 7 membered heterocyclic group optionally substituted by one R^{14} group;

each R^6 and R^7 is independently selected from H, $-C(O)(C_1-C_6$ alkyl), C_1-C_6 alkyl or $-(CH_2)_n(C_6-C_{10}$ aryl) wherein n is an integer from 0 to 2, and the foregoing aryl substituents are optionally substituted by 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, and azido;

$-NR^6R^7$ can be taken together to form the following structure



;

each R^8 is selected from the substituents provided in the definition of R^5 except R^8 is not H.

2. A compound acccording to claim 1 include those wherein R^3 is phenyl substituted by one $-CH_2NR^{11}R^{12}$ group and optionally substituted by 1 to 4 R^4 groups.

3. A compound according to claim 2 wherein said R^{11} and R^{12} groups are independently selected from C_1-C_{10} alkyl, $-(CR^6R^7)_m(C_6-C_{10}$ aryl), $-(CR^6R^7)_m(C_3-C_{10}$ cycloalkyl), indanyl and $-(CR^6R^7)_m$(4 to 10 membered heterocyclic), wherein m is an integer from 0 to 4, and the foregoing, R^{11} and R^{12} substituents, are optionally substituted by 1 to 3 substituents independently selected from halo, benzyl, trifluoromethyl, trifluoromethoxy, $-NR^6R^7$.

4. A compound according to claim 1 wherein one of the R^4 groups is halo and ortho to the ether oxygen.

5. A compound according to claim 4 wherein said halo group is chlorine.

6. A compound according to claim 1 wherein said compound is selected from the group consisting of:

3-(4-{(2S,3S,4S,5R)-5-[3-{2-chloro-4-[(methyl-napthalen-1—ylmethyl-amino)-methyl]-phenoxy}-1-methyl-(1E)-propenyl]-3,4-dihydroxy-tetrahydro-furan-2-yloxy}-3-hydroxy-phenyl)-2-methyl-N-((3aS,4R,5R,6S,7R,7aR)-4,6,7-trihydroxy-hexahydro-benzo[1,3]dioxol-5-yl)-(2E)-acrylamide;

3-(4-{(2S,3S,4S,5R)-5-[3-(4-benzylaminomethyl-2-chloro-phenoxy)-1-methyl-(1E)-propenyl]-3,4-dihydroxy-tetrahydro-furan-2-yloxy}-3-hydroxy-phenyl)-2-methyl-N-((3aS,4R,5R,6S,7R,7aR)-4,6,7-trihydroxy-hexahydro-benzo[1,3]dioxol-5-yl)-(2E)-acrylamide;

3-(4-{(-{(2S,4S,5R)-5-[3-(4-{[Benzyl-(2-dimethylamino-ethyl)-amino]-methyl}-2-chloro-phenoxy)-1-methyl-(1E)-propenyl]-4-hydroxy-tetrahydro-furan-2-yloxy}-3-hydroxy-phenyl)-2-methyl-N-((3aS,4R,5R,6S,7R,7aR)-4,6,7-trihydroxy-hexahydro-benzo[1,3]dioxol-5-yl)-acrylamide

3-(4-{(2S,3S,4S,5R)-5-[3-(2,3-Dichloro-4-{[(3-dimethylamino-propyl)-ethyl-amino]-methyl}-phenoxy)-1-methyl-propenyl]-3,4-dihydroxy-tetrahydro-furan-2-yloxy}-3-hydroxy-phenyl)-2-methyl-N-((3aS,4R,5R,6S,7R,7aR)-4,6,7-trihydroxy-hexahydro-benzo[1,3]dioxol-5-yl)-acrylamide

3-(4-{(2S,3S,4S,5R)-5-[3-(4-(3-chloro-benzyl)aminomethyl-2-chloro-phenoxy)-1-methyl-(1Z)-propenyl]-3,4-dihydroxy-tetrahydro-furan-2-yloxy}-3-hydroxy-phenyl)-2-methyl-N-((3aS,4R,5R,6S,7R,7aR)-4,6,7-trihydroxy-hexahydro-benzo[1,3]dioxol-5-yl)-(2E)-acrylamide;

3-(4-{(2S,3S,4S,5R)-5-[3-(4-ethylamino-2-chloro-phenoxy)-1-methyl-(1E)-propenyl]-3,4-dihydroxy-tetrahydro-furan-2-yloxy}-3-hydroxy-phenyl)-2-methyl-N-((3aS,4R,5R,6S,7R,7aR)-4,6,7-trihydroxy-hexahydro-benzo[1,3]dioxol-5-yl)-(2E)-acrylamide;

3-(4-{(2S,3S,4S,5R)-5-[3-(3-piperidinyl-2-chloro-phenoxy)-1-methyl-(1E)-propenyl]-3,4-dihydroxy-tetrahydro-furan-2-yloxy}-3-hydroxy-phenyl)-2-methyl-N-((3aS,4R,5R,6S,7R,7aR)-4,6,7-trihydroxy-hexahydro-benzo[1,3]dioxol-5-yl)-(2E)-acrylamide;

3-(4-{(2S,3S,4S,5R)-5-[3-(4-benzylaminomethyl-2-chloro-phenoxy)-1-methyl-(1E)-propenyl]-4-hydroxy-tetrahydro-furan-2-yloxy}-3-hydroxy-phenyl)-2-methyl-N-((3aS,4R,5R,6S,7R,7aR)-4,6,7-trihydroxy-hexahydro-benzo[1,3]dioxol-5-yl)-(2E)-acrylamide;

3-(4-{(2S,3S,4S,5R)-5-[3-{2-chloro-4-[(benzyl-methyl-amino)-methyl]-phenoxy}-1-methyl-(1E)-propenyl]-3,4-dihydroxy-tetrahydro-furan-2-yloxy}-3-hydroxy-phenyl)-2-methyl-N-((3aS,4R,5R,6S,7R,7aR)-4,6,7-trihydroxy-hexahydro-benzo[1,3]dioxol-5-yl)-(2E)-acrylamide;

3-(4-{(2S,3S,4S,5R)-5-[3-{2-chloro-4-[(ethyl-methyl-amino)-methyl]-phenoxy}-1-methyl-(1E)-propenyl]-3,4-dihydroxy-tetrahydro-furan-2-yloxy}-3-hydroxy-phenyl)-2-methyl-N-((3aS,4R,5R,6S,7R,7aR)-4,6,7-trihydroxy-hexahydro-benzo[1,3]dioxol-5-yl)-(2E)-acrylamide;

3-(4-{(2S,3S,4S,5R)-5-[3-{2-chloro-4-morpholin-4ylmethyl-phenoxy}-1-methyl-(1E)-propenyl]-3,4-dihydroxy-tetrahydro-furan-2-yloxy}-3-hydroxy-phenyl)-2-methyl-N-((3aS,4R,5R,6S,7R,7aR)-4,6,7-trihydroxy-hexahydro-benzo[1,3]dioxol-5-yl)-(2E)-acrylamide;

3-(4-{(2S,3S,4S,5R)-5-[3-(4-(3-chloro-benzyl)aminomethyl-2-chloro-phenoxy)-1-methyl-(1E)-propenyl]-3,4-dihydroxy-tetrahydro-furan-2-yloxy}-phenyl)-2-methyl-N-((3aS,4R,5R,6S,7R,7aR)-4,6,7-trihydroxy-hexahydro-benzo[1,3]dioxol-5-yl)-(2E)-acrylamide;

and the pharmaceutically acceptable salts, prodrugs and solvates of said compounds.

7. A pharmaceutical composition for the treatment of a bacterial infection, a protozoal infection, or a disorder related to a bacterial infection or a protozoal infection, in a

mammal, fish, or bird which comprises a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.

8. A method of treating a bacterial infection, a protozoal infection, or a disorder related to a bacterial infection or a protozoal infection, in a mammal, fish, or bird which comprises administering to said mammal, fish or bird a therapeutically effective amount of a compound of claim 1.